

THE EFFECTS OF DIFFERENT TYPES OF DIETS ON OBESE INDIVIDUALS DIAGNOSED WITH TYPE 2 DIABETICS

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ABSTRACT

The United Nation set out a goal to reduce poverty rates by 50% as part of its millennial goals, which was reached in 2010. Despite this reduction, attention is still given by organisations to decrease poverty further. Obesity was also mentioned in the UN report, however despite the global effort, its rate is increasing exponentially with projections of a billion adults being obese by 2025. Historically this has been explained by Maslow's hierarchy of needs which state that the most basic need of all people is food, which led to the belief that affordable food choices usually not as healthy as others and usually contains food groups which are known to contribute to obesity. Obesity can lead to diabetes which is likely preventable. This systematic review aim was to investigate the effect of food groups such as carbohydrate, protein and fat in different type of diets compared to the Mediterranean diet, to determine which diet provided the best benefit to decreasing fasting glucose, body mass index, waist circumference, low density cholesterol, systolic blood pressure levels as well as increasing high density cholesterol levels. This review concluded that low carbohydrate diet provided the best benefits compared to high protein, high fat and Mediterranean diet. A ketogenic diet was not as effective as standard low carbohydrate diet due to a risk of dehydration. Based on these findings, this review recommends that the best diet is that contains a combination of low carbohydrate, high protein and high fat.

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INTRODUCTION

The United Nations (UN), as part of its millennial goals, committed to halving poverty rates by 2015. In fact this was achieved by 2010[1]. Whilst worth celebrating, concurrently the rates of obesity increased. The organisation has stated that reducing diet-related diseases will not be achieved because around 1 billion of the global adult population are projected to be obese by 2025[2,3]. For the adult population in the UK, the prevalence of obesity increased from 13% of men and 16% of women in 1993 to 27% for both men and women in 2015[4]. Prehistorically, humans had to hunt for food or be hunted and consumed as much food as possible, preparing for the possible future famine. Those who survived were able to produce offspring, making the tendency to store large amounts of fat an evolutionary advantage. Based on Maslow's hierarchy of needs, food is a basic requirement for all humans [5]. The Metropolitan Life Insurance Company™ conducted a 25-year study on mortality rates amongst their policyholders. They identified that obesity was related to reduce life expectancy [6]. Nobody should consume excess food, or alcohol, or fast [7]. From the 1930s onwards, medical research into the negative effects of obesity increased providing the evidence base for current guidelines and policies.

Obesity increases risk of developing type 2 diabetes mellitus (T2DM), cancer, cardiovascular diseases (CVD), gallbladder disease, osteoarthritis and chronic back pain [8]. Evidence establishes links with endometrial, oesophageal adenocarcinoma, colorectal, postmenopausal breast, prostate and renal cancers [9]. The National Obesity Observatory stated: "severe obesity puts individuals at greater risk of depression" also noting stigma in relation to obesity in women who feel under pressure to be slim [10]. Obesity is also a risk factor for developing Alzheimer's disease. The Alzheimer's Society states; weakening of the fornix which connects the brain to the hippocampus to other brain regions, affects learning and memory [11]. Obesity is linked to T2DM is because of an increase of "non-esterified fatty acids, glycerol, hormones, cytokines, pro-inflammatory markers involved in the development of insulin resistance" [12].

In the UK overweight and obesity-related ill-health in 2014/15, cost £6.1 billion which exceeds the funding for the police, fire service, and judicial system combined [13]. The annual cost of hospital inpatient care for diabetes complications is estimated at between £1800 and £2500 per patient; annual outpatient costs between £300 and £370 per patient and the cost of medication to treat complications of diabetes is about 3-4 times the cost of the medications to treat the condition. This is leading to total diabetes expenditure of around £14 billion or

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£1.5 million per hour[14]. The UK is also falling behind in life expectancy for diabetic patients compared to other developed countries[15]. Currently around 90% of adults diagnosed with T2DM are overweight or obese [16]. Most of this personal and societal cost is considered potentially preventable; the most important advice is medication adherence and maintaining a healthy diet. However, controversy remains as to what might constitute a healthy diet.

Review Aim

The aim of this systematic review is to compare diets considered beneficial for obese T2DM.

The objective is to elucidate the best diet for obese T2DM patients through searching different databases to retrieve relevant studies. Once the primary studies on the different diets were identified, the common results of comparison were extracted and compared utilising RevMan5™ (Biostat, Englewood NJ), calculating the average mean for each category of comparison.

Study selection and calculation of risk of biases

All the selected studies featured participants with a mean body mass index (BMI) >30 except for Ellsworth *et al.*, (2016) where participants were allowed to enter the study with BMI of 25 and over [17]. All selected studies had quite small numbers of participants except; Coles *et al.*, (2014), Iqbal *et al.*, (2009), Shai *et al.*, (2008) and Lasa *et al.*, (2014) each had more than 100 participants [18,19,20,21]. The sample size is important because a low sample size corresponds to a reduction in confidence level which increases the risk of a large error of mean occurring. This affects reliability as it becomes less representative of the key population being investigated. Primary studies were retrieved from Embase™ and Pubmed™. Papers were excluded that investigated gestational diabetes or had no relation to the proposed primary objective (the effect of diet on co-existing obesity and diabetes). The Boolean operators, “And/or” weren’t applied as “diabetes” and “obesity” are rarely applied in combination. Studies were critically appraised and included in this review are listed at appendix 1.

The chosen sample represented the commonly used diets in diabetes patients. The first measurement analysed was the Glycated haemoglobin (HbA_{1c}). Body mass index (BMI) was chosen over a change in weight because it’s utilised to categorise participants into obese/overweight and correlates with a participant’s weight. Waist circumference (WP) was utilised as an alternative collaboration of weight loss. Also a visible decrease in waist circumference can motivate an obese participant to adhere to the prescribed intervention. Low-density lipids (LDL) and high-density lipids (HDL) levels and systolic blood pressure were used as indicative of the level of cardiovascular risk[22]. Table 1 shows the comparators used in this review to compare the selected studies’ findings.

Table 1 Primary studies that were found using the Search Strategy and the comparators that was used to analyse the results

Study	HbA _{1c}	BMI	WC	LDL	HDL	SBP
Brinkworth <i>et al.</i> , 2004	✓	×	×	✓	✓	✓
Coles <i>et al.</i> , 2014	✓	×	×	✓	✓	✓
Ellsworth <i>et al.</i> , 2016	×	✓	×	✓	✓	×
Fabricatore <i>et al.</i> , 2011	✓	×	✓	✓	✓	✓
Goday <i>et al.</i> , 2016	✓	✓	✓	✓	✓	×
Gumbiner <i>et al.</i> , 1996	×	×	×	×	×	×
Iqbal <i>et al.</i> , 2009	✓	×	×	✓	✓	✓

Lasa <i>et al.</i> , 2014	×	✓	✓	×	×	×
Malin <i>et al.</i> , 2007	×	×	×	×	×	×
Miyashita <i>et al.</i> , 2004	×	×	×	×	×	×
Papakonstantinou <i>et al.</i> , 2010	✓	✓	✓	✓	✓	✓
Saslow <i>et al.</i> , 2014	✓	✓	×	✓	✓	✓
Shai <i>et al.</i> , 2008	✓	✓	✓	✓	✓	✓
Tay <i>et al.</i> , 2014	✓	✓	✓	✓	✓	✓
Watson <i>et al.</i> , 2016	✓	✓	✓	✓	✓	✓
Westman <i>et al.</i> , 2008	✓	✓	✓	✓	✓	✓

*HbA_{1c}: Glycosylated Haemoglobin, BMI: body mass index, WC: Waist Circumference, LDL: low density cholesterol, HDL: high density cholesterol, SBP: systolic blood pressure
The Cochrane™ Handbook for Systematic Reviews of Interventions was used to guide the design of this review. The CONSORT™ check list was utilised to appraise the studies and analysis was conducted using RevMan5™.

Figure 1 is a summary of the risk of bias that was concluded from analysis all the studies employing CONSORT.

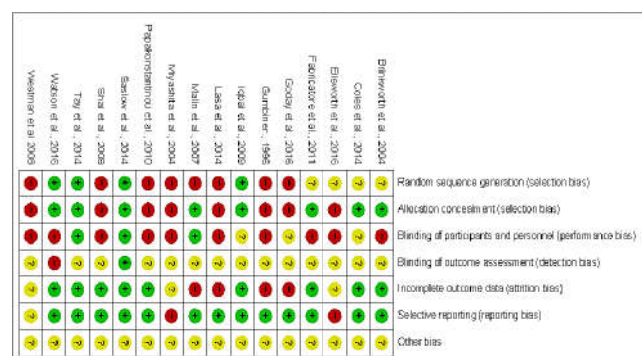


Figure 1 Risk of bias summary for the primary studies

FINDINGS AND DISCUSSION

The Effect of Diets on HbA_{1c} levels

The mean difference (Figure 2) below is used to describe the difference between the means reported for the high and low carbohydrate diets respectively. In this case, it is clear low-carbohydrate diets decrease HbA_{1c} levels more than high-carbohydrate diets. The outcome for Saslow *et al.*, (2014) was not included in the RevMan5 analysis to prevent skewed results [23]. The analysis found that the low-carbohydrate diet had significant effect on HbA_{1c} with a mean difference of 0.6.

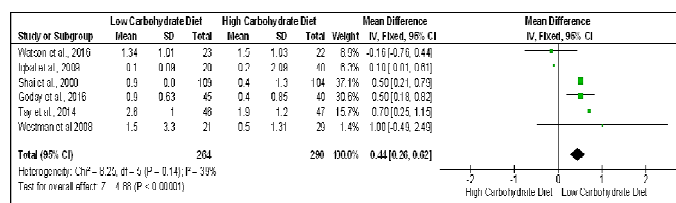


Figure 2 The effect of carbohydrate diet on HbA_{1c} levels (%)

High-protein diet reduced HbA_{1c}, but the effect was smaller than low-carbohydrate diets (Figure 3). This is confirmed as Watson *et al.*, (2016) investigated carbohydrate and protein diets as the low-carbohydrate diet featured a higher protein content [24].

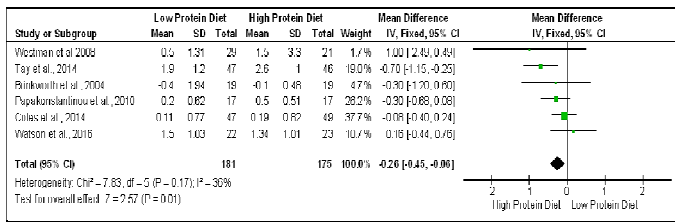


Figure 3 The effect of protein diet on HbA1c levels (%)

Only two studies investigated the effect of Mediterranean diets on HbA1c levels. The conclusion is that a non-Mediterranean diet induced a better decrease in HbA1c than Mediterranean diets (Figure 4).

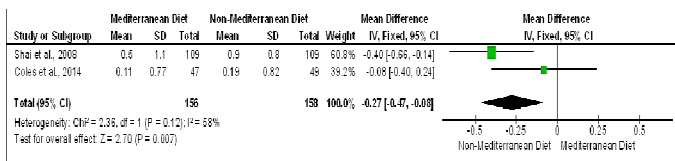


Figure 4 The effect of Mediterranean diet on HbA1c levels (%)

The result for the effect of fat diets on HbA1c indicates that high-fat diets were the least effective in level reduction (Figure 5) compared to all others (figures 2, 3 and 4). In this analysis the Saslow *et al.*, (2014), study was also excluded.

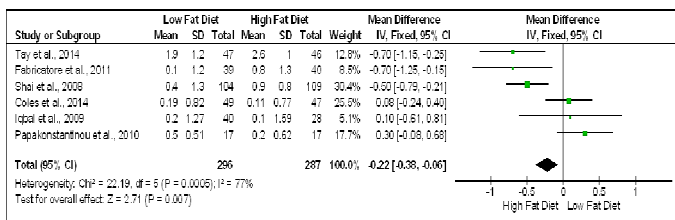


Figure 5 Figure 3D - The effect of fat diet on HbA1c levels (%)

The effect of diets on BMI

The results demonstrated that the low-carbohydrate diet also provided a decrease in BMI and therefore a decrease in weight. All the studies apart from Tay *et al.*, (2014) and Shai *et al.*, (2008) reported a decrease in BMI in compared to the high carbohydrate diet [25,20]. Westman *et al.*, (2008) had a low p-value as the SD wasn't calculated and because of this, the SD was high causing a large range in this calculation (Figure 6).

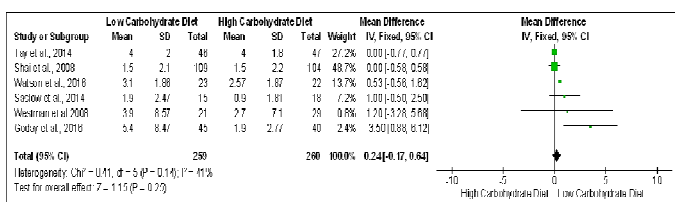


Figure 6 The effect of carbohydrate diet on BMI levels (/m2)

The first two studies suggested that high protein diets decrease BMI but the last two studies, which feature a smaller range, induced a mean difference of 0. Because of this, the mean difference skewed towards high protein diets decreasing BMI but not compared to the low carbohydrate result. The most concerning result is Westman *et al.*, (2008) (Figure 7).

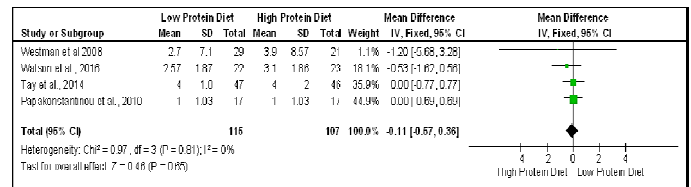


Figure 7 The effect of protein diet on BMI levels (/m2)

Due to the Ellsworth *et al.*, (2016) having a small p-value, the SD was increased dramatically and is most likely an anomalous result. The reason the mean value was extremely low despite the huge mean difference reported in Ellsworth *et al.*, (2016), the enormous confidence interval gives it a low overall weight. The Mediterranean diet has minimal effect on reducing BMI levels (Figure 8).

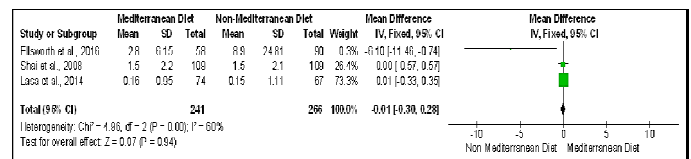


Figure 8 The effect of Mediterranean diet on BMI levels (/m2)

High-fat diets were the most effective in reducing BMI levels compared to all others. Lasa *et al.*, (2014) reported the largest change in BMI for high-fat diets compared to low-fat diets which is why it was weighted higher compared to Shai *et al.*, (2008) and Tay *et al.*, (2014) results. This is interesting considering Tay *et al.*, (2014) and Papakonstantinou *et al.*, (2010) showed no difference in the effect of high and low-fat diets on BMI (Figure 9) [25,26].

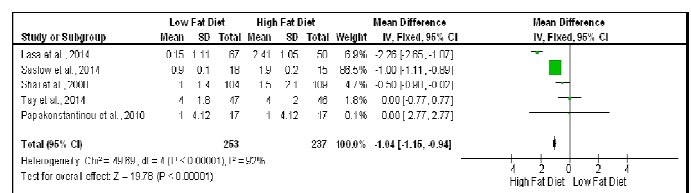


Figure 9 The effect of fat diet on BMI levels (/m2)

The Effect of diet on Waist Circumference

The low-carbohydrate diet favours a decrease in waist size. Westman *et al.*, (2008) reported their results waist circumference in inches whilst the others were reported in centimetre (cm), so a decision was made to convert their results to cm to sustain consistency (Figure 10).

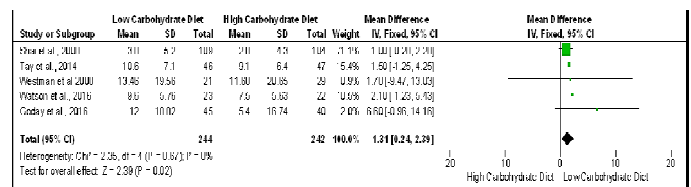


Figure 10 The effect of carbohydrate diet on waist circumference (cm)

The results show no effect for protein content on waist circumference (Figure 11).

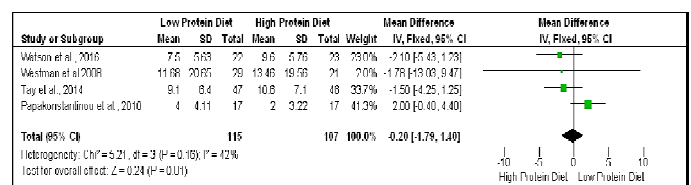


Figure 11 The effect of protein diet on waist circumference (cm)

The results for Lasa *et al.*, (2014) (Figure 12) were combined as results for males and females were recorded separately. The results show no effect for Mediterranean diets on waist circumference.

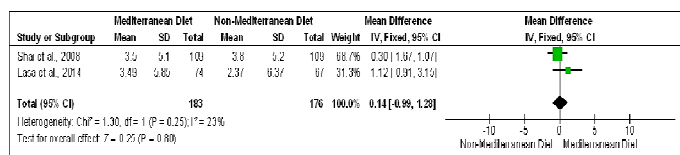


Figure 12 The effect of Mediterranean diet on waist circumference (cm)

The high-fat result exhibited the second largest decrease in results of the studies reported here. However the confidence interval for the combined result crosses the index.

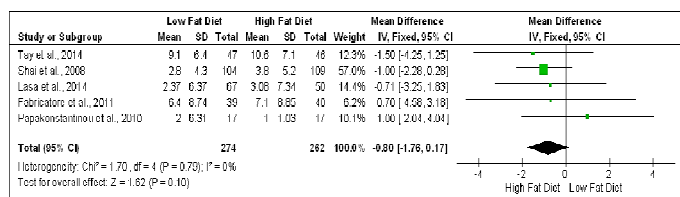


Figure 13 The effect of fat diet on waist circumference (cm)

The effect of diet on LDL cholesterol

Westman *et al.*, (2008) featured a negative result because it represented the only result to exhibit that a high-carbohydrate diet increased LDL level. The cholesterol results for Goday *et al.*, (2016), Iqbal *et al.*, (2009) and Shai *et al.*, (2008) had to be converted from mg/dl to mmol/L to keep the results consistent. Overall, the high carbohydrate diet appears the most effective at reducing LDL cholesterol (Figure 14).

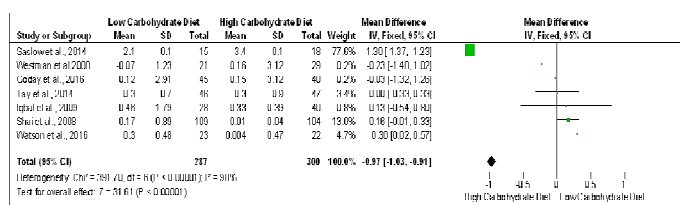


Figure 14 The effect carbohydrate diet on LDL cholesterol (mmol/L)

The protein content of the diet showed no significant effect on cholesterol levels (Figure 15).

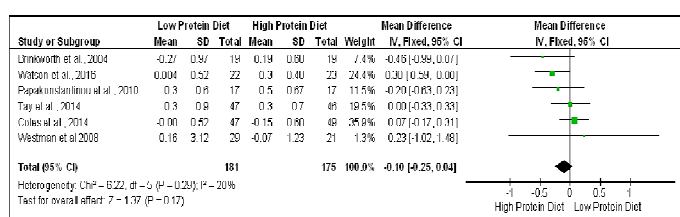


Figure 15 The effect of protein diets on LDL cholesterol (mmol/L)

Similarly there was no effect for the Mediterranean diet on cholesterol levels (Figure 16).

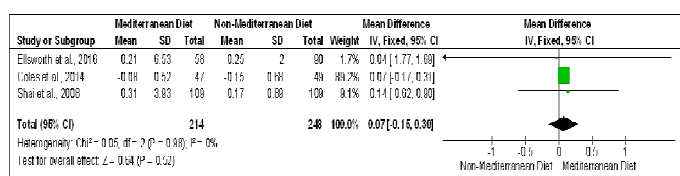


Figure 16 The effect of Mediterranean diets on LDL cholesterol (mmol/L)

The low-fat diet was effective at reducing LDL cholesterol compared to the high carbohydrate diet (Figure 17).

Fabricatore *et al.*, (2011) and Coles *et al.*, (2014) found low-fat diets marginally increased LDL cholesterol levels, but the effects noted in the other studies were conclusive [18,27].

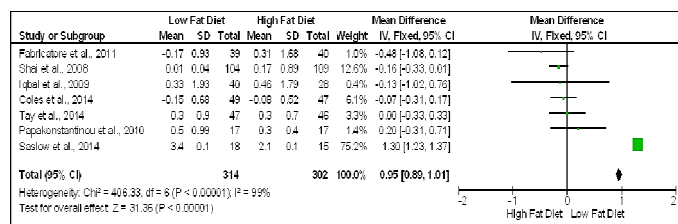


Figure 17 The effect of fat diets on LDL cholesterol (mmol/L)

The effect of diets on HDL cholesterol

Low carbohydrate diets were effective in increasing HDL compared to high-carbohydrate diet (Figure 18). What stands out is three studies cross the decision line but the overall effect is clear. Saslow *et al.*, (2014) and Westman *et al.*, (2008) were excluded as they did not have HDL levels.

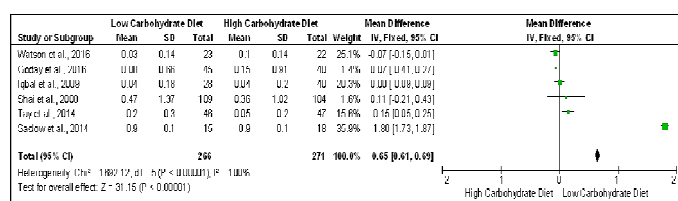


Figure 18 The effect of carbohydrate diet on HDL cholesterol (mmol/L)

Clearly the protein in the diet showed no effect on cholesterol levels. (Figure 19). Papakonstantinou *et al.*, (2010) was excluded.

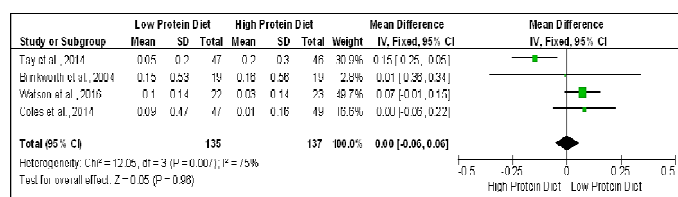


Figure 19 The effect of protein diets on HDL cholesterol (mmol/L)

Mediterranean diets have a slightly better effect on increasing HDL levels compared to non-Mediterranean diets, but it was not large enough to be considered significant because it's marginally larger (Figure 20).

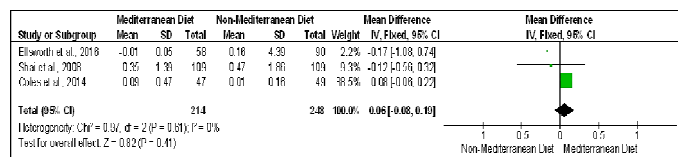


Figure 20 The effect of Mediterranean diet on HDL cholesterol levels (mmol/L)

The definitive conclusion that can be made is that low-fat diets are better in increasing HDL levels compared to high-fat diets as well as low-carbohydrate levels (Figure 21). This is a little surprising considering the first four studies recorded results in favour of the high-fat diet. Saslow *et al.*, (2014) was included in this analysis. Papakonstantinou *et al.* (2010) wasn't included due to the high fat diet having no effect on HDL decrease but there was a slight decrease seen in the lower fat diet.

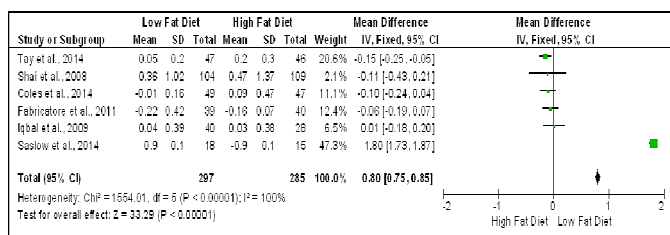


Figure 21 The effect of fat diet on HDL cholesterol (mmol/L)

The effect of diets on systolic BP

Low-carbohydrate diets featured a better decrease in BP compared to higher carbohydrate diets (Figure 22). When looking at the results, the ranges were comparatively different for each study ranging from a 0.6 to 6.7 with the only study favouring a decrease in BP for high carbohydrate diet being Shai *et al.*, (2008).

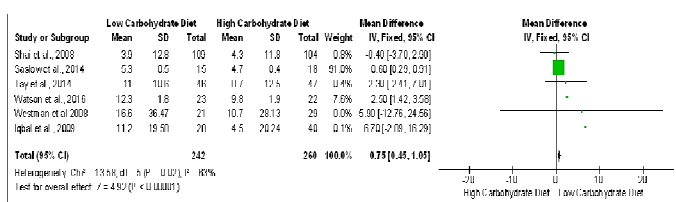


Figure 22 The effect of carbohydrate diet on systolic BP (mmHg)

The results showed that a higher protein diet causes a large decrease in systolic BP and this effect is large compared to the effect that a low-carbohydrate diet featured on systolic BP (Figure 23). The ranges that were reported were even larger compared to the ones that low-carbohydrate ones sustained which ranged from 0.5 to 8.30.

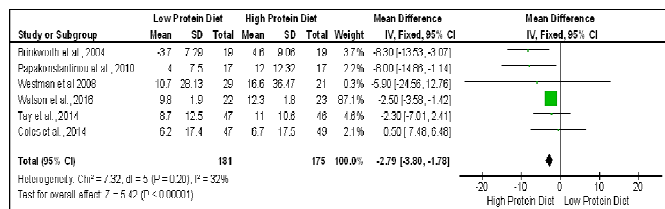


Figure 23 The effect of protein diet on systolic BP (mmHg)

The Mediterranean diet depicted a better decrease in systolic BP compared to the low-carbohydrate diet, although, only two studies recorded the effects of systolic BP for this. What doesn't aid the results embodied when Coles *et al.*, (2014) reported non-Mediterranean diet being better for reducing BP and Shai *et al.*, (2008) recording the opposite. The results favoured Shai *et al.*, (2008) because Shai *et al.*, 2008 featured a larger sample size meaning that its effect size will be better than Coles *et al.*, (2014) even if 96 participants is still a reasonable sample size (Figure 24).

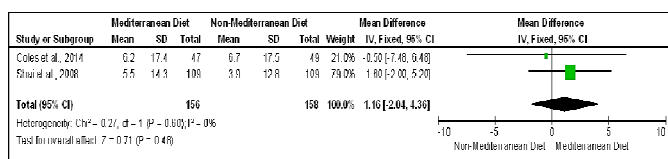


Figure 24 The effect of Mediterranean diet on systolic BP (mmHg)

Finally, low-fat diets established a better decrease in systolic BP compared to higher-fat diet, but this effect is smaller compared to the other diets. The interesting thing to note is how both diets have results with pronounced effect with Iqbal

et al., (2009) favouring the high-fat diet and Fabricatore *et al.*, (2011) favouring the lower fat diet (Figure 25).

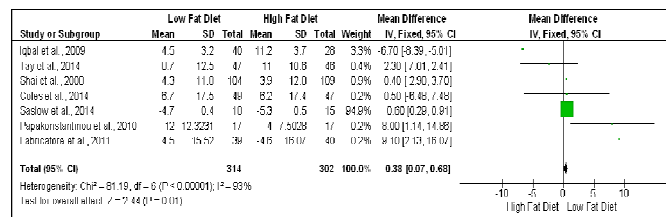


Figure 25 The effect of fat diet on systolic BP (mmHg)

Appendix 1 Primary studies from the search strategy

- Brinkworth *et al.*, 2004
- Brinkworth, G., Noakes, M., Parker, B., Foster, P. and Clifton, P. (2004). Long-term effects of advice to consume a high-protein, low-fat diet, rather than a conventional weight-loss diet, in obese adults with Type 2 diabetes: one-year follow-up of a randomised trial. *Diabetologia*, 47(10), pp.1677-1686.
- Coles *et al.*, 2014
- Coles, L., Fletcher, E., Galbraith, C. and Clifton, P. (2014). Patient freedom to choose a weight loss diet in the treatment of overweight and obesity: a randomized dietary intervention in type 2 diabetes and pre-diabetes. *International Journal of Behavioral Nutrition and Physical Activity*, 11(1), p.64.
- Ellsworth *et al.*, 2016
- Ellsworth, D., Costantino, N., Blackburn, H., Engler, R., Kashani, M. and Vernalis, M. (2016). Lifestyle modification interventions differing in intensity and dietary stringency improve insulin resistance through changes in lipoprotein profiles. *Obesity Science & Practice*, 2(3), pp.282-292.
- Fabricatore *et al.*, 2011
- Fabricatore, A., Wadden, T., Ebbeling, C., Thomas, J., Stallings, V., Schwartz, S. and Ludwig, D. (2011). Targeting dietary fat or glycemic load in the treatment of obesity and type 2 diabetes: A randomized controlled trial. *Diabetes Research and Clinical Practice*, 92(1), pp.37-45.
- Goday *et al.*, 2016
- Goday, A., Bellido, D., Sajoux, I., Crujeiras, A., Burguera, B., García-Luna, P., Oleaga, A., Moreno, B. and Casanueva, F. (2016). Short-term safety, tolerability and efficacy of a very low-calorie-ketogenic diet interventional weight loss program versus hypocaloric diet in patients with type 2 diabetes mellitus.
- Gumbiner *et al.*, 1996
- Gumbiner, B., Wendel, J. and McDermott, M. (1996). Effects of diet composition and ketosis on glycemia during very-low-energy-diet therapy in obese patients with non-insulin-dependent diabetes mellitus. *The American Journal of Clinical Nutrition*, 63(1), pp.110-115.
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obesity. Diabetes Research and Clinical Practice, 65(3), pp.235-241.

- Papakonstantinou, E., Triantafyllidou, D., Panagiotakos, D., Koutsovasilis, A., Saliaris, M., Manolis, A., Melidonis, A. and Zampelas, A. (2010). A high-protein low-fat diet is more effective in improving blood pressure and triglycerides in calorie-restricted obese individuals with newly diagnosed type 2 diabetes. *European Journal of Clinical Nutrition*, 64(6), pp.595-602.
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CONCLUSION

The studies that investigated carbohydrate diets in comparison to others featured a consistent result concluding that low-carbohydrate diets produced a favourable reduction in obesity and glucose levels [19,20,23,24,25,28]. The only study that disagreed with this conclusion was Watson *et al.*, (2016) who argued that high-carbohydrate diets were as effective as low-carbohydrate diets [29].

Shai *et al.*, (2008) and Iqbal *et al.*, (2009) concluded that low-carbohydrates were superior to low-fat diets. Brinkworth *et al.*, (2004) also investigated the high and low-protein and fat diet, they concluded that fat content had no effect at all [30]. The studies that investigated Mediterranean diet, Shai *et al.*, (2008), Coles *et al.*, (2004) and Lasa *et al.*, (2004) all featured over 100 participants in their trial providing greater reliability in their findings compared to studies with fewer participants. Shai *et al.*, (2008) concluded that a low-carbohydrate and the Mediterranean diet are superior to low-fat diets due to a more favourable effect on glycemic levels. Coles (2004) reported that men preferred being directed to their choice of diet (the non-Mediterranean diet) compared to females who preferred having a choice (including Mediterranean diet), (Coles *et al.*, 2004). Finally, Lasa *et al.*, (2014) concluded that Mediterranean diets improved glucose metabolism but to the same extent as low-fat diets. Additionally, whole-grain diets, ketogenic diets and vegetarian diets were included in some of the studies used in this review. The whole-grain diet study by Malin *et al.*, (2007) concluded that the whole-grain diet reduced the risk of attaining diabetes compared to refined-grain diets [31]. A very-low-calorie ketogenic diet was compared to a hypocaloric diet by Goday *et al.*, (2016) which concluded that the very-low ketogenic diet was more effective [32]. Furthermore, Gumbiner, Wendel, and McDermott (1996) investigated high-ketogenic very-low-energy diets against low-ketogenic diets and concluded the former induced better glycemic effects than the latter [33]. Finally, Ellsworth *et al.*, (2016) compared a strict vegetarian diet against a Mediterranean-style diet on insulin resistant in T2DM and concluded both were equally as effective. Protein diets have always been something that has been associated with bodybuilding so it was assumed there will be a benefit for all individuals including diabetic patients, however, this was not the case. The high protein diet “reduces hunger, improves satiety, increases thermogenesis” and whilst a higher protein intake does not increase plasma glucose, it can “increase insulin response” which may be a problem for patients with T2DM because of insulin resistance. Therefore, if a high protein diet were to be recommended, the amount to be taken has to at least correspond to a person’s body weight and not exceed that to prevent harm [34]. The third diet that had an impact on obesity was the low-fat diet, but this result was barely more effective when compared to the high-fat diet. When talking about fat, it’s important to remember that the fat discussed is trans-fat as they increase LDL levels, decrease HDL levels and increase the ratio of triglycerides to HDL cholesterol as well as increasing triglycerides. Overall, these contribute to an increased risk of cardiovascular disease from occurring due to atherosclerosis [35]. However, there also exist unsaturated fats that sustain levels of HDL cholesterol whilst reducing LDL cholesterol [36]. “Fatty acids influence glucose metabolism by altering cell membrane function, enzyme activity, insulin signalling, and gene expression”. Due to this, the evidence has consistently suggested that “replacing

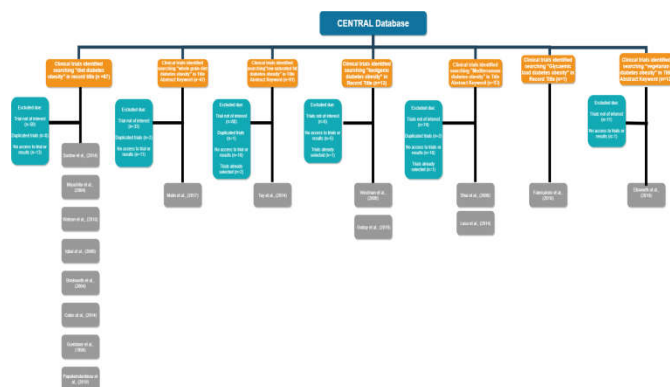


Figure 1 Flow chart representing filters applied to CENTRAL database to find the clinical trials with the exclusion criteria

Limitation

There are few trials that compared the Mediterranean diet, accordingly, the results may have swung towards Mediterranean diets having a better benefit for those participants as it was a diet most recommended for obese people in general.

saturated fats and trans fatty acids with unsaturated fats have beneficial effects on insulin sensitivity and are likely to reduce the risk of type 2 diabetes" [37]. Finally, the diet that experienced the least impact was the Mediterranean diets, although, the Mediterranean diet was comparable to the high-fat diet. Whilst Mediterranean diet did not make a significant impact on obesity in patients diagnosed with diabetes, there is evidence that suggests they're beneficial for obese patients with diabetes, the effect isn't as significant compared to the rest of the diets and could be suggested as an alternative. In conclusion, the systematic review identified the low carbohydrate (not low enough to induce ketosis), high protein diet and high unsaturated fat diet, in this order, is the best possible choices. Overall, there are large numbers of diets claiming to be superior to others but also addressing different aspects such as healthy living, weight management, cardiovascular benefit, muscular appearance benefit, energy benefit, and the list goes for very long. Regardless of a diet type, balanced nutrition that can be followed long term and produce health benefit outcomes is the best diet for patients with a chronic condition.

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